
Methylome-wide Analysis of Chronic HIV Infection Reveals Five-Year Increase in Biological Age and Epigenetic Targeting of HLA.

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Public Summary:

HIV-infected individuals are living longer on antiretroviral therapy, but many patients display signs that in some ways resemble premature aging. To investigate and quantify the impact of chronic HIV infection on aging, we report a global analysis of the whole-blood DNA methylomes of 137 HIV+ individuals under sustained therapy along with 44 matched HIV- individuals. First, we develop and validate epigenetic models of aging that are independent of blood cell composition. Using these models, we find that both chronic and recent HIV infection lead to an average aging advancement of 4.9 years, increasing expected mortality risk by 19%. In addition, sustained infection results in global deregulation of the methylome across >80,000 CpGs and specific hypomethylation of the region encoding the human leukocyte antigen locus (HLA). We find that decreased HLA methylation is predictive of lower CD4 / CD8 T cell ratio, linking molecular aging, epigenetic regulation, and disease progression.

Scientific Abstract:

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